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# Dapivirine Ring: Regulatory Update

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Zeda Rosenberg, IPM

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# Presentation Outline

- Phase III and Open-Label Results: Summary
- Regulatory Overview
- Additional Ring Research
- Global Product Access

# Phase III and Open-Label Results: Summary



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# Phase III Results Summary



- IPM's monthly dapivirine ring **reduced HIV-1 risk by approximately 30% overall** and was **well-tolerated**
- Participants who used the ring at least some of the time saw their **HIV infection risk cut by 45%**
- **Greater HIV risk reduction was associated with increased ring use**
- Overall, women over age 21 saw their HIV risk reduced by 40%; women under 21 saw no reduction
- More research needed to understand prevention needs of younger women





# OLE Studies: Interim Results

**Similar across both OLEs (as of Oct. 2017):**

- Safety profile similar to Phase III trials
- Adherence to ring use increased:
  - 83% in Ring Study to 96% in DREAM
  - 77% in ASPIRE to 89% in HOPE
- Modelling data suggest women's HIV-1 risk reduced by ~50% in both OLEs
- Interim data suggest ring use and risk reduction increase when participants know Phase III results

**New DREAM interim data to be presented at R4P 2018 (poster presentation)**

# Regulatory Overview



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# Path to Regulatory Approval

**IPM is the dapivirine ring's regulatory sponsor and:**

- Holds worldwide rights to dapivirine
- Ensures all preclinical, clinical and pharmaceutical quality/chemistry, manufacturing and controls (CMC) data meet regulatory requirements
- Is formally applying for approval through European, African and US regulatory authorities



# Regulatory Application Requirements

- **Many countries have different application formats**
  - Same types of data required, from early preclinical lab tests through safety and efficacy trials
- **IPM's master dapivirine ring dossier allows customized applications to specific global and African NRAs**
  - 13 years of data and findings from nearly 250 studies
  - Contains 260K PDF pages — enough to fill a 2x2 meter room printed!



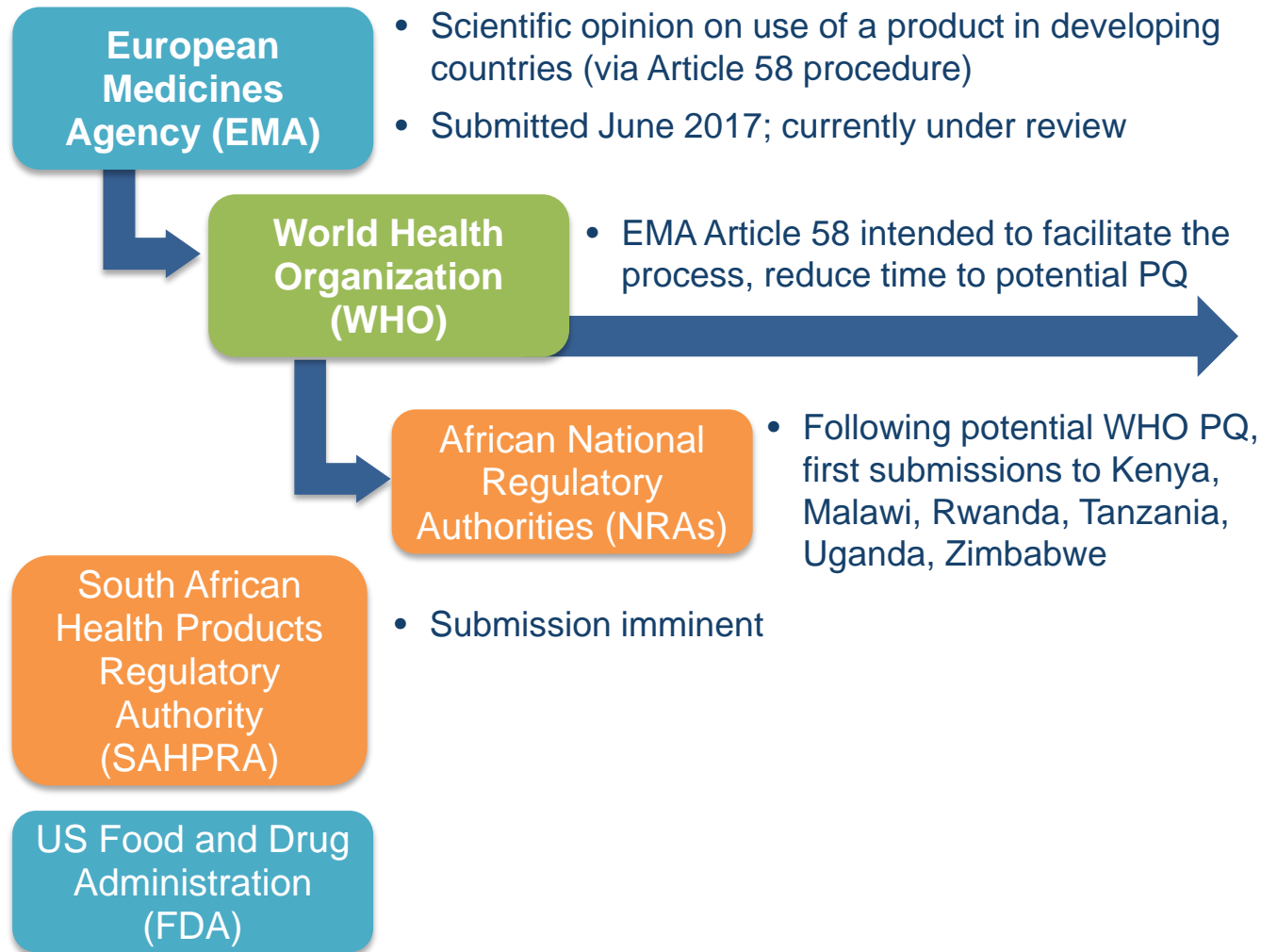


# The Regulatory Dossier

The global dossier includes all data on the dapivirine ring:

- **Product quality (CMC)**
  - Janssen and IPM preclinical study data
- **Safety and Pharmacology**
  - Janssen and IPM preclinical study data
  - IPM and MTN safety clinical trial data
  - Integrated safety data from clinical trials
  - Pharmacokinetic data from IPM clinical trials
- **Efficacy**
  - Integrated efficacy data from Phase III trials
  - Preliminary data from OLEs (DREAM and HOPE)

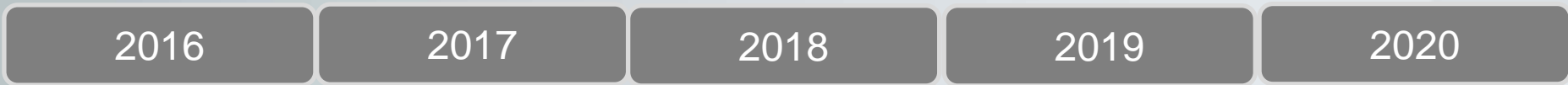
# Regulatory Overview



## Why WHO pre-qualification?

- ✓ Evaluates whether a drug meets global standards for quality, safety, efficacy
- ✓ Many African NRAs consider EMA's scientific opinion and WHO PQ status in their own reviews
- ✓ Could facilitate policy development

# Projected Regulatory Timelines



**Phase 3 Results**

Open-label extension study: DREAM

Open-label extension study: HOPE



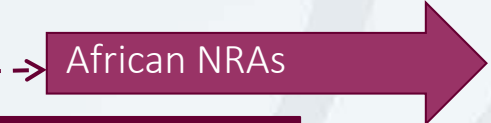
African adolescents safety study: REACH

Supporting safety and PK studies

Safety studies in pregnant and breastfeeding women

EMA Article 58

WHO PQ



US FDA

S. Afr. (SAHPRA)



# WHO Prequalification and Policy Development



## WHO PQ can facilitate supportive policy environments

- WHO public health guidelines
  - Can take 9-12 months
- Essential Medicines Lists (EML)
  - Informs national EMLs and purchasing decisions

# Additional Ring Research



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# Women's Needs Vary During Their Lives

- **Women's circumstances change over time**
- **Women need new options they could use at different times of their lives:**
  - For women wanting contraception
  - For women wanting to conceive
  - For women who are pregnant or breastfeeding



# Additional Dapivirine Ring Research

- **REACH adolescent study**
  - Safety and use of dapivirine ring and oral PrEP among 300 young women ages 16-21 in Kenya, South Africa, Uganda, Zimbabwe; to begin early 2019
- **Pregnant and breastfeeding women**
  - Safety and acceptability studies of ring and PrEP in Africa in 2019
- **3-month dapivirine ring**
  - Phase I clinical trial began 2017; results expected 2019
- **3-month dapivirine-levonorgestrel ring**
  - Phase I clinical trial began in 2017; results to be presented at R4P 2018
  - Second Phase I trial began in 2018



# Global Product Access

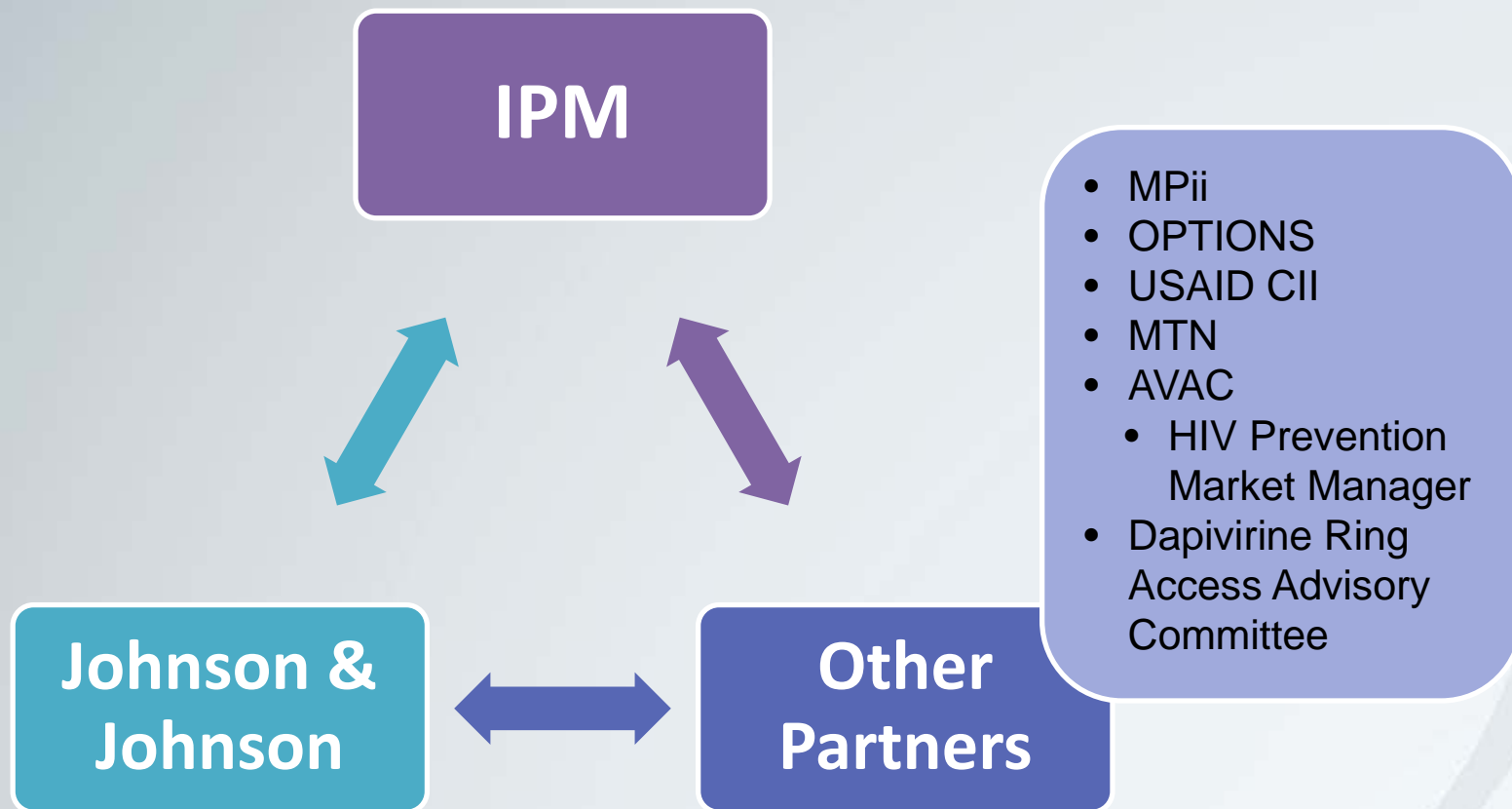


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# Access Collaborations for Successful Product Introduction



# Dapivirine Ring Access Advisory Committee

- **Established Sept. 2017**
- **12 experts across sectors, primarily from Africa**
- **Purpose:** To help ensure successful market introduction and long-term adoption of the dapivirine ring
- **Approach:** Provide advice on plans, activities and partnerships to ensure IPM's access strategy is shaped by the insights and expertise of adolescent girls, women, communities, program implementers and health experts



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International Community of Women  
Living with HIV Eastern Africa (ICWEA)



an affiliate of Johns Hopkins University



# Dapivirine Ring Access Strategy: Key Components

## Government & Donor Support

Incorporation of the ring into guideline and funding decisions



## Clinic/Hospital Access

Drive awareness and education of the ring to encourage HCP referrals to end-users



## DPV Ring Market Access Strategy

## Operations & Logistics

Craft strategy to deliver the ring in-country to clinics/hospitals via appropriate channels and partnerships



## End-User Access

Drive awareness, education and use of the ring among women



# Healthcare Provider Research



**Goal:** Build healthcare provider knowledge of dapivirine ring to ensure it is prescribed and used properly

- **Objectives:**
  - Identify potential providers who will be involved in ring introduction
  - Understand and assess knowledge of and attitudes toward ring
  - Understand end-user pathway
- **Methods:** Interviews and focus group discussions with clinical health providers, community health workers, health ministry officials
- **Locations:** South Africa, Zimbabwe, Uganda, Malawi, Kenya, Rwanda, Tanzania
- **Status:** Completed in Rwanda, report pending; planned in Malawi
- **Findings will inform IEC materials & implementation planning**
- **Partners:** J&J Global Public Health and Genesis

# End-user Market Segmentation Research









**Goal:** Develop thorough understanding of end-user preferences and needs

- **Objectives:** Identify and differentiate potential ring users
- **Methods:** Qualitative and quantitative research with women ages 15-45 and male influencers ages 18-55
- **Locations:** Malawi, South Africa, Uganda and Zimbabwe
- **Status:** Phase I interviews completed in Uganda, with findings to inform Phase II; planning for South Africa fieldwork
- **Partners:** J&J Global Public Health, Busara, Thinkplace



# Cross-Country Assessment for Ring Potential

	ZIMBABWE	UGANDA	SOUTH AFRICA	KENYA	MALAWI	TANZANIA	RWANDA
 <b>HIV epidemic characteristics</b>	SIGNIFICANT NEED	SIGNIFICANT NEED	SIGNIFICANT NEED	SIGNIFICANT NEED	SIGNIFICANT NEED	SIGNIFICANT NEED	MODERATE NEED
<i>Prevalence rate</i>	13.5%	6.5%	18.8%	4.8%	9.2%	4.7%	3.1%
<i>New infections annually</i>	40,000	52,000	270,000	53,000	36,000	55,000	7,500
<i>Incidence rate</i>	3.03	1.50	5.46	1.21	2.29	1.19	0.70
 <b>HIV prevention program</b>	STRONG OPPORTUNITY	STRONG OPPORTUNITY	STRONG OPPORTUNITY	STRONG OPPORTUNITY	MODERATE OPPORTUNITY	MODERATE OPPORTUNITY	MODERATE OPPORTUNITY
 <b>Oral PrEP experience</b>	STRONG OPPORTUNITY	MODERATE OPPORTUNITY	STRONG OPPORTUNITY	STRONG OPPORTUNITY	POTENTIAL LIMITATION	MODERATE OPPORTUNITY	MODERATE OPPORTUNITY
 <b>Ring trial experience to-date</b>	STRONG OPPORTUNITY	STRONG OPPORTUNITY	STRONG OPPORTUNITY	MODERATE OPPORTUNITY	MODERATE OPPORTUNITY	POTENTIAL LIMITATION	POTENTIAL LIMITATION
 <b>Stakeholder reactions to the ring</b>	STRONG OPPORTUNITY	STRONG OPPORTUNITY	MODERATE OPPORTUNITY	STRONG OPPORTUNITY	MODERATE OPPORTUNITY	MODERATE OPPORTUNITY	MODERATE OPPORTUNITY
 <b>Product introduction process</b>	STRONG OPPORTUNITY	STRONG OPPORTUNITY	MODERATE OPPORTUNITY	MODERATE OPPORTUNITY	MODERATE OPPORTUNITY	POTENTIAL LIMITATION	STRONG OPPORTUNITY

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